will be presented and compared to a control autograft population. Deacetylase inhibition post autograft may have both clinical efficacy and immunomodulatory activity.

126

BORTEZOMIB AND HIGH DOSE MELPHALAN FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (B-HDM/SCT) FOR THE TREATMENT OF AL AMYLOIDOSIS: RESULTS OF A FEASIBILITY STUDY

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Aggressive treatment of AL amyloidosis with high dose melphalan and autologous stem cell transplant (HDM/SCT) is effective in inducing hematologic remission and clinical improvement. We have observed in ~ 500 patients treated with HDM/SCT that achievement of a hematologic complete response (CR) is a critical determinant of clinical improvement and survival. A synergistic effect between bortezomib (B) and melphalan has been demonstrated in vitro and in vivo. Thus, the combination of B and HDM is a logical approach to study. Because of the importance of hematologic CR in treatment outcome, we conducted a feasibility study to determine whether addition of B to HDM/SCT would be tolerable and would increase hematologic CR rates. Eligibility for entry into the trial required diagnosis of AL amyloidosis, age > 18 years, and adequate performance status (SWOG ≤ 2) and cardiopulmonary function (LVEF > 45%, DLCO > 50%). Peripheral blood stem cells were collected following G-CSF mobilization, with minimum yields of 2.5×10^6 CD34+ cells/kg required for participation in the trial. B was administered at 1 mg/m^2 on D -6, D -3, D +1, and D +4 and HDM at 140-200 mg/m^2 in two divided doses on D -2 and D -1. From 10/2008 to 10/2009, 9 patients were enrolled (median age 53, range 46-68; median number of involved organs 2, range 1-4). Of the 9 patients enrolled, 1 patient was removed from the protocol because of cardiac arrhythmia during stem cell mobilization and collection phase that precluded treatment with HDM/SCT. Of the 8 patients who received B-HDM/SCT, there was no treatment-related mortality within 100 days of SCT and there were no unexpected hematologic or non-hematologic toxicities associated with addition of B to HDM/SCT. The median times to neutrophil and platelet engraftment was D +10 and D +14 after SCT, respectively. Of 8 patients evaluable for early responses, normalization of serum free light chain levels and ratio occurred in 7 of 8 (88%) by D +14 and one patient achieved a 45% reduction in serum free light chain concentration at D +14. Of the initial 2 patients with longer follow-up, both have achieved a hematologic CR at 6 and 9 months following B-HDM/SCT. Follow-up is ongoing and hematologic responses appear to be well-maintained. Thus, this pilot study demonstrates that B-HDM/SCT is tolerable for selected patients with AL amyloidosis and leads to a high rate of hematologic responses.

127

TRANSPLANT ASSOCIATED-THROMBOTIC MICROANGIOPATHY (TA-TMA) IN PEDIATRIC NEUROBLASTOMA (NB) PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT): A CASE-CONTROL STUDY IDENTIFYING EARLY CLINICAL MARKERS OF DISEASE

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Patients (pts) undergoing ASCT for NB present a unique population to study TA-TMA due to their standardized chemotherapy, lack of graft-versus host disease prophylaxis, and subsequent exposure to radiation and cis-retinoic acid (cisRA). We performed a retrospective case-control study of TA-TMA in NB pts who underwent ASCT at CCHMC in the past 5 years to identify strategies for early rigorous diagnosis. Twenty pts with high risk NB were treated with melphalan, carboplatin, and etoposide followed by ASCT. Six pts were diagnosed with TA-TMA (4 within 25 days of ASCT) presenting with microangiopathic hemolytic anemia, elevated lactate dehydrogenase, thrombocytopenia, hypertension (HTN), and acute kidney injury (3 confirmed with renal biopsy). Adenovirus, cytomegalovirus, and influenza B were potential triggers of TA-TMA (n = 2). The 14 pts without TA-TMA served as controls. Clinical and laboratory data were obtained for the first 30 days pre- and post-ASCT. Blood pressure (BP) index was calculated as BP/95th percentiles for age and height (value >1 = HTN). No pt had HTN pre-ASCT. Fischer's exact test, Wilcoxon rank sum and generalized linear models were used for analysis. Results are shown in the Table. Proteinuria, hematuria, and schistocytes on blood smear were significantly associated with TA-TMA, while blood and platelet transfusions were not. HTN requiring therapy proved to be a very significant indicator of TA-TMA and was identified within days of ASCT. Although serum creatinine (SCr) did not differ significantly between groups, pts with TA-TMA had an average 60% decrease in renal function from baseline by nuclear glomerular filtration rate (nucGFR) post ASCT, compared to a 30% decrease in those without TA-TMA. TA-TMA therapy included steroids, plasmapheresis, and rituximab. There was no TA-TMA-related mortality, but significant complications included progression to chronic dialysis (n = 1) and severe polyserositis (n = 2). None of the pts with TA-TMA were able to complete cisRA therapy. Overall, we found a 30% prevalence of TA-TMA in transplanted NB pts. The most significant indicator of TA-TMA was HTN. Our data are limited by their retrospective nature and small sample size. We suggest that careful BP observation and urinalysis monitoring will assist in the early diagnosis of TA-TMA, while SCr measurements are of limited value. Prospective studies are needed to confirm these results as early diagnosis and treatment may eventually help to improve outcome.

Indicators of TA-TMA during first month post-ASCT

Variable	TA-TMA (n = 6)	No TA-TMA (n = 14)	P-value
Proteinuria	4 (67%)	2 (15%)	0.046
Hematuria	4 (67%)	1 (8%)	0.02
Schistocytes	4 (67%)	1 (8%)	0.02
Pre-ASCT NucGFR	152.0 ± 12.9	145.6 ± 10.9	0.64
Post-ASCT NucGFR*	61.0 ± 8.8	103.1 ± 6.2	0.002
SCr (mg/dL)	0.54 ± 0.04	0.49 ± 0.02	0.28
Systolic BP (mm Hg)	112.2 ± 2.5	102.2 ± 1.6	0.004
Diastolic BP (mm Hg)	66.7 ± 2.2	55.4 ± 1.5	0.001
Systolic Index	1.02 ± 0.02	0.92 ± 0.02	0.002
Diastolic Index	0.99 ± 0.04	0.81 ± 0.02	0.001
Pts requiring HTN therapy	5 (83%)	3 (21%)	0.006

Data n (%) or mean ± standard error. *NucGFR (ml/min/1.73 m^2) done on average 61 days post-ASCT

128

IS LOW DOSE CYCLOPHOSPHAMIDE PLUS G-CSF MOBLIZATION AS EFFECTIVE AS MOZOBIL (PLERIXAFOR) PLUS G-CSF IN MULTIPLE MYELOMA (MM) PATIENTS ELIGIBLE FOR TANDEM TRANSPLANT?

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Introduction: A recent study showed 71.6% of patients who received plerixafor plus G-CSF collected >6 × 10^6 CD34+ cells/kg in ≤ 2 apheresis procedures when compared to placebo plus G-CSF. We analyzed retrospectively two tandem autologous transplant protocols where cyclophosphamide plus G-CSF (Cy-G) was used as mobilization therapy.

Methods: From 08/1999 to 06/2009, 120 MM patients were enrolled. Patients received 1.5 g/m^2 of Cy followed by G-CSF. Patients underwent consecutive leukapheresis starting on day 10 and continued until a minimum of 4x 10^6 CD34+/kg was collected and 6 × 10^6 CD34+/kg when possible.

Results: Median days to reach 4x 10^6 CD34+/kg was 1 (1-16) and for 6 × 10^6 CD34+/kg was 2 (1-16). Median days of total apheresis was 3

(1-16). Median total CD34+/kg collected was 9.98 × 10^6 (2.55-35.79). Twenty-six (25%) patients had prior radiation. Median age was 54.4 years, range 29.7-66.1. Median days to neutrophil engraftment was 11, range 1-16 post first transplant and 10 days (8-43) post second transplant. Days to platelet independence after first transplant was 13 days (0-71), and 12 days (0-44) after the second. We found that time from diagnosis to collection (≤7 months vs ≥ 7 months) impacted reaching the 6 × 10^6 CD34+ cells/kg within the 1-2 days target. Our analysis showed that patients apheresed <7 months from diagnosis were 2.6 times (CI: 1.14-5.95) more likely to reach 6 × 10^6 CD34+/kg within the 1-2 days (p = 0.02). This result is comparable to those of DiPersio et al, Blood 113 (23):5720-5726, 2009. Sixty-seven percent of our Cy-G patients reached 6 × 10^6 CD34+/kg in 2 days vs 71.6% of DiPersio's plerixafor-G pts.
Conclusion: CD34+ cell yield following Cy-G mobilization is comparable to what could be obtained with plerixafor-G mobilization. We suggest reserving plerixafor for patients with substantial delay between diagnosis and apheresis and for those failing Cy-G mobilization.

129

COMPARATIVE COST-EFFECTIVENESS OF PLERIXAFOR PLUS GRANULOCYTE-COLONY STIMULATING FACTOR VERSUS CYCLOPHOSPHAMIDE PLUS GRANULOCYTE-COLONY STIMULATING FOR AUTOLOGOUS PERIPHERAL BLOOD STEM CELL MOBILIZATION IN PATIENTS WITH NON-HODGKIN'S LYMPHOMA

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Introduction: Chemomobilization of autologous peripheral blood stem cells (PBSCs) is costly and requires substantial resource allocations. This burden has considerable effects on patients (pts), providers and payers. We performed a retrospective study to evaluate the difference in costs and effectiveness of first-line mobilization of autologous PBSCs with cyclophosphamide (CY; 1.5-4 gm/m^2) + G-CSF (n = 34) versus plerixafor + G-CSF (n = 8) in pts with non-Hodgkin's lymphoma (NHL) between 6/2006 and 8/2009.
Methods: We created a decision analytic model to estimate the mean costs and effectiveness rates for the two regimens. This model incorporated the minimum acceptable CD34+ cell dose for autologous PBSC transplant (PBSCT) and also incorporated adverse events such as clinically significant nausea and vomiting, anemia, thrombocytopenia, and hospital admissions for neutropenic fever. The analysis was conducted from the perspective of a managed care organization and used published literature to identify drug, laboratory, and apheresis costs. A treatment success was defined as adequate CD34+ dose to proceed with autologous PBSCT. We conducted a Monte Carlo simulation of 1,000 cases.
Results: Successful PBSC mobilization occurred in 24 of 34 pts (70.6%) in the CY group and in 7 of 8 pts (87.5%) in the plerixafor group. Nine of the 10 pts who failed CY proceeded to second-line plerixafor. Two pts in the CY group and one pt in the plerixafor group underwent allogeneic transplant after failing autologous PBSC mobilization (estimated cost $400,000; not included in analysis). For CY + G-CSF, the mean cost was $20,965 and the mean effectiveness was 0.71; for plerixafor + G-CSF, the mean cost was $19,523 and the mean effectiveness was 0.87. The Monte Carlo simulation showed overlap between the two regimens in the 95% confidence intervals in both cost and effectiveness. The incremental analysis demonstrated that plerixafor + G-CSF dominated CY + G-CSF (i.e., plerixafor and G-CSF was more effective and less costly) in 69.9% of cases.
Conclusion: This decision analytic model demonstrates that plerixafor + G-CSF is more cost-effective than CY + G-CSF for autologous PBSC mobilization in most pts with NHL. This analysis, conducted from a managed care perspective, does not consider the effects of the two PBSC mobilization strategies on the quality of life in these pts. Similar decision analyses in pts undergoing PBSC mobilization for myeloma could also be instructive.

130

A COMPARISON OF TOXICITY AND MOBILIZATION EFFICACY FOLLOWING TWO DIFFERENT DOSES OF CYCLOPHOSPHAMIDE FOR MOBILIZATION OF HEMATOPOIETIC STEM CELLS IN NON-HODGKIN'S LYMPHOMA PATIENTS

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Background: Cyclophosphamide (Cy) (2-7 g/m^2) has been shown to be an effective regimen for hematopoietic stem cell (HSC) mobilization in Non-Hodgkin's Lymphoma (NHL) patients undergoing autologous stem cell transplantation (ASCT). However, the optimal dose to be used, which maximizes HSC collection yields while minimizing febrile neutropenia and other toxicities, remains controversial. Two historical cohorts of NHL patients who received G-CSF and Cy at dose of either 4 g/m^2 (Cy4) or 2 g/m^2 (Cy2) were compared.
Methods: 56 patients undergoing first mobilization with Cy and G-CSF at a single institution between 6/06 and 9/09 were retrospectively analyzed. The initial Cy4 patient cohort (n = 28) was mobilized with Cy 4gm/m^2 starting on Day 1 followed by G-CSF 10ug/kg/day starting on Day 7 and continuing until completion of apheresis. Beginning in 2/08, the Cy dose was reduced to 2gm/m^2 and the G-CSF start date was moved to day 4 (Cy2 n = 28). Minimal and optimal yield was defined as collection of ≥2 × 10^6 and ≥5 × 10^6 CD34+ cells/kg respectively. Prophylactic antibiotics were given for ANC <500 to reduce risk of febrile neutropenia.
Results: Minimal cell dose required for ASCT was achieved in 96% vs. 68% of Cy4 and Cy2 patients, respectively (p = 0.0116). The one patient failing to mobilize following Cy4, later collected a minimal cell dose following G-CSF and plerixafor. Of the 9 patients failing to mobilize on Cy2, six of these subsequently mobilized minimal yields following G-CSF and plerixafor. Median number of apheresis required was significantly lower in the Cy4 patients (2 vs.3, p = 0.0085). The proportion of patients collecting the minimal and optimal cell dose in 2 or fewer days of apheresis was 82% vs.39% (p = 0.0022) and 46% vs.14% (p = 0.0186), in the Cy4 and Cy2 patients respectively. Mobilization with Cy4 was associated with a significantly higher incidence of hospital admissions due to febrile neutropenia (32% vs. 0%, p = 0.018), which prompted the change from Cy4 to Cy2.
Conclusions: Although Cy4 and Cy2 are both effective HSC mobilizing regimens, mobilization efficacy and toxicity vary greatly. Cy4 results in higher HSC yields requiring fewer apheresis procedures, but this benefit is offset by increased morbidity and hospitalization. Based on the suboptimal results with Cy 4 g/m^2 and Cy 2 g/m^2 mobilization, we are currently exploring Cytoxan 3gm/m^2 in hopes to balance mobilization safety, efficacy and cost.

	Cy 4gm/m2 + G-CSF n = 28	Cy 2gm/m2 + G-CSF n = 28	P Value
% of Patients who achieved ≥ 2 x10^6 CD34+ cells/kg in day ≤ 2	82% (23/28)	39% (11/28)	0.0022
% of Patients who achieved ≥ 5 x 10^6 CD34+cells/kg in ≤ 2 days	46% (13/28)	14% (4/28)	0.0186
% of Patients who achieved ≥ 5 x10^6 CD34+cells/kg	64% (18/28)	18% (5/28)	0.009
% of Patients who collected ≥ 2 x 10^6 CD34+ cells/kg	96% (27/28)	68% (19/28)	0.0116
Median (range) days of collection in all patients	2 (1-5)	3 (1-7)	0.0085
% Patients hospitalized for febrile neutropenia	32% (9/28)	0%	0.018